

REMARKS

Claim Amendments

Claims 1, 2, 4-10 and 13 were subject to the action. Claims 5, 7 10 and 13 are canceled. Claims 1, 6, 8 and 9 are amended. New claims 14-16 are added. Claims 1, 2, 4, 6, 8, 9 and 14-16 are subject to examination.

Claim 1 is amended to provide that Claim R_2 , R_3 , R_4 , R_5 and R_6 can be hydrogen. This is a retraction of the amendment made in the response dated November 13, 2007 that erroneously removing hydrogen from the Markush group.

Claims 6, 8 and 9 are amended to change dependency, and to correct antecedent basis.

New claim 14 depends from claim 1 and provides that the cyanine further comprises a biomolecule conjugated through the linker arm $-R_1-C\equiv CH$. Support is from original claim 5.

New claim 15 depends from claim 1 and provides that the cyanine further comprises a second fluorescent dye conjugated through the linker arm $-R_1-C\equiv CH$. Support is from original claim 7.

New claim 16 depends from claim 1 and provides that the cyanine further comprises a first biomolecule conjugated through the linker arm $-R_1-C\equiv CH$ and a second equal or different biomolecule conjugated through the linker arm $-R_8-Y$. Support is from original claim 10.

No new matter has been added by way of the claim amendments.

Restriction and Election

Applicant acknowledges the selection for examination of species **Group XVII**, identified in Applicant's response dated November 13, 2007.

Applicant requests reconsideration and withdrawal of the restriction of claims 5-10 (now claims 6, 8, 9 and 14-16).

Applicants election of Group XVII, with traverse, identified cyanine with two differently-functionalized linkers, and its conjugates with biomarkers and fluorescent dye. The election of Group XVII was made without distinction between the compound and conjugates thereof, and without restriction to specific claims, such that Applicant's election included all claims of the

application. Applicant's response dated November 13, 2007 traversed the Examiner's determination that had stated that the inventions of the application "are no so linked as to form a single general inventive concept". The present Action states "(t)he Office has accepted Applicant's counter restriction requirement, and withdraw the previous restriction requirement dated on 10/12/07" (emphasis added). 37 CFR 1.142(b) states that the "(c)laims to the invention or inventions not elected, if not canceled, are nevertheless withdrawn from further consideration by the examiner by the election, subject however to reinstatement in the event the requirement for restriction is withdrawn or overruled." Since the initial restriction has been withdrawn, all claims, elected or not, should have been reinstated and made subject to examination, subject to any further restriction requirement that the Examiner may make.

The examiner's alleged restriction in the present action of Claims 5-10 has not been identified by the examiner as a new restriction. Claims to the cyanine (claims 1, 2 and 4) and the the conjugate cyanine (claims 6, 8, 9 and 14-16) may be considered subcombination and combinations. MPEP 806.05(c) - Criteria of Distinctness Between Combination and Subcombination, provides that

"(t)o support a requirement for restriction between combination and subcombination inventions, both two-way distinctness and reasons for insisting on restriction are necessary, i.e., there would be a serious search burden if restriction were not required as evidenced by separate classification, status, or field of search... The inventions are distinct if it can be shown that a combination as claimed:

(A) does not require the particulars of the subcombination as claimed for patentability (to show novelty and unobviousness), and

(B) the subcombination can be shown to have utility either by itself or in another materially different combination."

Since the present action provides no support for any further restriction requirement, and does not provide any reasons for restricting the combination from the subcombination, claims 5-10 (now claims 6, 8, 9 and 14-16) should be reinstated and examined, until such time that a proper restriction requirement is made.

Furthermore, in view of the present amendments and arguments, the claims 1, 2 and 4 appears to be patentable over the prior art of record, whereby the remaining non-elected subject matter, including claims 6, 8, 9 and 14-16 should be examined.

Incorporation of Foreign Priority Claim

The rejection on page 4 under “Specification” seems to state that the applicant must amend the specification to included the foreign priority claim to PZ2003000002. With all due respect, Applicant is not aware of any requirement of identifying foreign priority applications within the specification, and request the examiner to clarify the requirement by pointing out any such requirement under the law or rules.

Claim rejection under 35 USC §101

Claim 13 is rejected as non-statutory subject matter, for covering a use.

Claim 13 has been canceled without prejudice, thereby rendering moot the rejection.

Claim rejection under 35 USC §112

Claim 13 is rejected as being indefinite, for failing to set forth any steps involved in the method of use.

Claim 13 has been canceled without prejudice, thereby rendering moot the rejection.

Claim rejection under 35 USC §103

Claims 1, 2, 4 and 13 are rejected as obvious over Gaputo (US2002/065421 or the “421 application”) in view of Takashima et al (US2002/0051926 or the “926 application”), and Stavrianopolous et al (US2003/0225247 or “247 application”).

Applicant traverses.

The rejection ascertained that the difference between the prior art and the claimed invention was that the '421 application discloses an indocyanine dye substituent of alkyl bonding to the indole ring, but not an alkyne ($-R1 \equiv CH$). (see Action page 8 lines 6-9). The finding of a prima facie obviousness rejection was based solely upon that single difference between the prior art and the claimed invention.

Applicant respectfully notes that Claim 1 requires that "one of R_2 , R_3 , R_4 , R_5 and R_6 is $-R_8-Y$ ", and that a substituent group " $-R_8-Y$ " could not be identifies at any position on the rings of the "indocyanine dye 4a" of the '421 application.

On the contrary, Applicant notes that the '421 application teaches that "[o]f the different indolenines employed in these syntheses, the more reactive are those not bearing electron withdrawing groups in the benzene ring or with additional condensed benzene rings and with simple alkyl chains attached to the quaternary nitrogen." ('421 application paragraph [0014] lines 11-15, emphasis added). The '421 application goes on to teach that "[a] decrease in reactivity is observed when these cyanines bear carboxylalkyl or sulfonatoalkyl chains or electron withdrawing groups in the benzene ring, such as sulfonic or carboxylic groups. A similar decrease in reactivity is also observed with cyanines bearing additional condensed benzene rings. The least reactive cyanines are those with additional condensed benzene rings bearing sulfonic groups and quaternised with sulfoalkyl or carboxylalkyl groups." ('421 application paragraph [0014] lines 16-21, emphasis added).

As a consequence, the '421 application does not disclose, and rather teaches away from, this feature, because compounds with "carboxylalkyl or sulfonatoalkyl chains or electron withdrawing groups in the benzene ring" would decrease the reactivity of the indolenines and defeat the purpose of the "general strategy synthesis" taught in the '421 application's paragraph [0014]. Applicant notes that neither the '926 application nor the 247 application disclose such substitution. Since "(a)ll words in a claim must be considered in judging the patentability of that claim against the prior art." (*In re Wilson*, 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970)), Applicant submits accordingly that the rejection has failed to make a *prima facie* case of obviousness because the cited references fail to teach, suggest or make obvious all the features of the claims.

In view of the above, the Applicant submits that independent claim 1 is patentable over the cited art, together with claims depending therefrom, at least by virtue of their dependency.

Applicant asserts that Claims 6, 8, 9 and new claims 14-16, which include all the limitations of the cyanine of claim 1, are likewise patentable over the cited prior art.

Double patenting

The Examiner rejects claims 1-2, 4 and 13 on the ground of non-statutory obviousness-type double patenting as being unpatentable over claims 1-11 of US Patent 6,136,612 (the '612 patent). (Claim 13 is now canceled.)

Applicant traverses.

The rejection first appears to suffer in form, because the rationale for the rejection appears to also rely upon the alleged teaching of the aforementioned "926 application" and "247 application".

Nevertheless, Applicant respectfully points out that Claim 1 requires that "one of R_2 , R_3 , R_4 , R_5 and R_6 is $-R_8-Y$ ". A substituent group " $-R_8-Y$ " could not be identified at any position on the indocyanine rings of the compounds of the '612 patent.

Accordingly, the Applicant submits that the rejection fails to make a *prima facie* case of obviousness between the present application and the '612 patent, and that the present application and the '612 patent are patentably distinct, at least for substantially the same reasons indicated in the remarks related to the 35 USC §103 rejection, above.

In view of the above, the Applicant submits that independent claim 1, and is patentable over the cited art, together with claims depending therefrom, at least by virtue of their dependency.

Claim objections

The Examiner objects to Claims 1-2, 4 and 13 as containing both elected and non-elected subject matter.

Applicant understands that, should the elected subject matter be allowed, the Examiner would extend examination to the non-elected embodiments contained in New Group II. In view of the present amendments and arguments, the elected subject matter appears to be patentable over the prior art of record, and Applicant requests that the remaining non-elected subject matter of the claims be examined.

The Examiner is respectfully requested to otherwise clarify the objection.

CONCLUSION

Applicant believes a full and complete response to the Action has been made. In view of the above amendments and remarks, allowance of all the claims is respectfully requested.

Respectfully submitted,

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